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(54) Title: PSEUDOTYPED RETROVIRUSES AND STABLE CELL LINES FOR THEIR PRODUCTION

(57) Abstract

Cells that produce inventive pseudotyped retroviruses having a broad host range have been produced. In one aspect of the invention, the cells produce retroviruses pseudotyped with at least two different viral glycoproteins, such as togaviral glycoproteins. In alternative embodiments, the cells produce retroviruses pseudotyped with filoviral glycoproteins. Methods of producing the above-described cells, as well as the pseudotyped retroviruses thus produced, are also provided. In other embodiments, methods of screening agents effective in blocking viral entry into a cell, including filoviral entry or entry of viruses having at least two different viral glycoproteins disposed in their lipid bilayer, such as togaviruses, are provided. Moreover, methods of using the inventive pseudotyped retroviruses for introducing nucleotide sequences into target cells, and kits for forming the inventive pseudotyped retroviruses, are also provided.

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# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/17702

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) :C12P 21/06; C12N 7/04, 5/00; A61K 39/12
US CL :435/69.1, 236, 325; 424/199.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.1, 236, 325; 424/199.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

USPATFUL, MEDLINE, WEST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| Y | US 5,491,084 A (CHALFIE et al.) 13 February 1996, see entire document. | 3-4 |
| Y | US 5,512,421 A (BURNS et al.) 30 April 1996, see entire document. | 1-12 |
| Y | US 5,591,624 A (BARBER et al.) 07 January 1997, see entire document. | 1-12 |
| Y | US 5,503,974 A (GRUBER et al.) 02 April 1996, see entire document. | 1-12 |
| Y | US 5,723,287 A (RUSSELL et al.) 03 March 1998, see entire document. | 1-12 |
| Y | US 5,278,056 A (BANK et al.) 11 January 1994, see entire document. | 1-12 |

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 25 JANUARY 2000 | 10 FEB 2000 |
| Name and mailing address of the ISA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231<br>Facsimile No. (703) 305-3230 | Authorized officer<br>Jeffrey S. Parkin, Ph.D.<br>Telephone No. (703) 308-0196 |

Form PCT/ISA/210 (second sheet)(July 1992)★

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/17702

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| Y | US 5,185,440 A (DAVIS et al.) 09 February 1993, see entire document. | 5-7 |
| Y | LOPEZ, S. et al. Nucleocapsid-Glycoprotein Interactions Required for Assembly of Alphaviruses. J. Virol. March 1994, Vol. 68, No. 3, pages 1316-1323, see entire document. | 5-7 |
| Y | KUHN, R. J. et al. Chimeric Sindbis-Ross River Viruses to Study Interactions between Alphavirus Nonstructural and Structural Regions. J. Virol. November 1996, Vol. 70, No. 11, pages 7900-7909, see entire document. | 5-7 |

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/17702

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-12

**Remark on Protest**

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/17702

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-12, drawn to a eukaryotic cell comprising nucleotide sequences encoding, inter alia, at least two different viral glycoproteins.
Group II, claim(s) 13-18, drawn to a eukaryotic cell comprising nucleotide sequences encoding, inter alia, a filoviral glycoprotein.
Group III, claim(s) 19-29, drawn to a method of producing a eukaryotic cell capable of producing pseudotyped retroviruses with two different viral glycoproteins.
Group IV, claim(s) 30-32, drawn to a method of producing a eukaryotic cell capable of producing pseudotyped retroviruses with a filoviral glycoprotein.
Group V, claim(s) 33-38, drawn to a pseudotyped retrovirus containing at least two different viral glycoproteins.
Group VI, claim(s) 39, drawn to a pseudotyped retrovirus containing a Marburg virus glycoprotein.
Group VII, claim(s) 40-43, drawn to a method of introducing a nucleotide sequence into a cell by transducing a cell with a pseudotyped retrovirus expressing at least two different viral glycoproteins.
Group VIII, claim(s) 44, drawn to a method of introducing a nucleotide sequence into a cell by transducing a cell with a pseudotyped retrovirus expressing a Marburg virus glycoprotein.
Group IX, claim(s) 45-49 and 51, drawn to a method of screening for agents effective in blocking viral entry employing a pseudotyped retrovirus expressing at least two different viral glycoproteins.
Group X, claim(s) 50, 52, and 54, drawn to a method of screening agents effective in blocking Marburg virus entry into a cell employing a pseudotyped retrovirus expressing a Marburg virus glycoprotein.
Group XI, claim(s) 53, drawn to a kit for forming pseudotyped retroviruses containing at least two different viral glycoproteins.
Group XII, claim(s) 55, drawn to a kit for forming psuedotyped retroviruses containing a Marburg virus glycoprotein.

The inventions listed as Groups I-XII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The claims are directed toward multiple products (e.g., eukaryotic cells, pseudotyped retroviral particles, kits) with different chemical structures/compositions and attendant features (e.g., expressing two different viral glycoproteins, expressing a single virus glycoprotein). The claims are also directed toward multiple methods (e.g., method of making a eukaryotic cell capable of producing retroviral pseudotypes, method of gene transduction employing pseudotyped retroviral particles, method of screening for putative antiviral agents) that employ different reagents, methodology steps, and accomplish different scientific objectives. Accordingly, the claims all lack a special technical feature and are directed toward different inventive concepts.